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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/742,675	12/20/2000	Martin Stocks	18396/1490	4900
29933	7590	06/15/2004	EXAMINER	
PALMER & DODGE, LLP KATHLEEN M. WILLIAMS 111 HUNTINGTON AVENUE BOSTON, MA 02199			MCGARRY, SEAN	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

**Application No.**

09/742,675

**Applicant(s)**

STOCKS ET AL.

**Examiner**

Sean R McGarry

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

Applicant submission of foreign priority papers is acknowledged. Applicants claim of benefit of 60/090,867 is also acknowledged.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 15, 16 and 17 all recite (and the remaining claims all depend therefrom) "stable hybrid". It is noted that this term is a relative term and the specification provides no basis for the determination of what would be considered a stable hybrid in the context of the instant invention. The metes and bounds of the claims has not been clearly set forth with the use of this relative terminology.

Claim 7 is unclear. It is unclear what is meant by "becomes energetically favourable", for example. What becomes more energetically favorable, and further, more favorable for what?

Claim 18 recites "in said target or non-target nucleic acid", there is no antecedent basis for this recitation in the claims.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal et al [WO 94/01550].

Agrawal et al discloses antisense oligonucleotides that are “self stabilized”.

Agrawal et al disclose antisense that have a first region and a second region that bind a target sequence wherein the first region is available for binding while the second region is temporarily “masked” (See page 5, lines 13-25, for example). On page 7 and in Figures 1, 2, 5, and 6, for example it is disclosed the “masking through a hairpin structure. The above Figures and the above cites also disclose that a first region (hybridizing region) is complementary to a target sequence and is in single stranded form and at least Figure 1 shows that the first region is within the region of 3-18 bases in length (See also pages 9-10 which discloses a preferred range of 8-50 nucleotides in length for the hybridization target region/first region). Figure 7 show a ribozyme, targeted to HIV gag mRNA, with a hairpin region. The ribozyme has a “first” region, the 5' hybridizing arm, which is available for hybridization. Since the “first” region is 10 nucleotides in length it is “insufficiently long to provide stable binding by itself”, as per applicants disclosure page 9, lines 3-5. It is noted that since the region is 10 nucleotides in length, the region of Agrawals' ribozyme would appear to be of an advantageous

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length. The second region, the 3' hybridizing arm, is temporarily masked in the absence of a target. It is noted that the 3' hybridizing region, the second region of the instant invention, contains a 3' portion that makes a hairpin structure and this is a non-target region (ie is not the HIV gag mRNA), however, it is complementary to the "second region" of the molecule, for example. Further, at least Figure 1 discloses that the self-complementary region/second region is complementary to a sequence of the target sequence that is contiguous with that targeted by a first region/hybridizations region. It has been taught that the self-stabilized oligonucleotides can target single stranded and double stranded targets, for example (see page 10, for example). At least at pages 8 and 16 it is disclosed that the self-stabilized oligonucleotides can be composed of RNA, DNA, or combinations thereof, for example. The inhibition of expression of target sequences is disclosed at pages 9-13, for example. It is noted that at page 9 of Agrawal et al it is disclosed that the "disruption and replacement of base-pairing takes place because the intermolecular base-paired structure formed by the hybrid between the target nucleic acid sequence and the target hybridization region is more thermodynamically stable than the intra-molecular base-paired structure formed by the self-complementary oligonucleotide." The instant specification asserts at page 7, in its broad definition of "stabilizing elements", that the aim of the elements is to render the second region/target hybrid more stable than the second region in its masked state. Since Agrawal et al have disclosed this characteristic in the self-stabilized oligonucleotide these oligonucleotides, without evidence to the contrary, inherently contain some destabilizing element.

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Applicant's arguments filed 3/24/04 have been fully considered but they are not persuasive. Applicant argues that the claimed invention is defined over the prior art since the claims at hand recite "of insufficient length to form a stable hybrid with the target molecule". It is noted that this position is not agreed with as evidenced by the new grounds of rejection above. It is noted that the instant specification provides a basis for what constitutes a region "of insufficient length to form a stable hybrid with the target molecule" at page 9, lines 3-5. It is noted that the prior art relied upon meets this definition and is properly applied. Since The ribozyme of Agrawal contains two such regions targeting the same target it is the position of the examiner that it would be considered stable, see Figure 7 which shows the combination of the two regions having 20 base pair interaction, for example.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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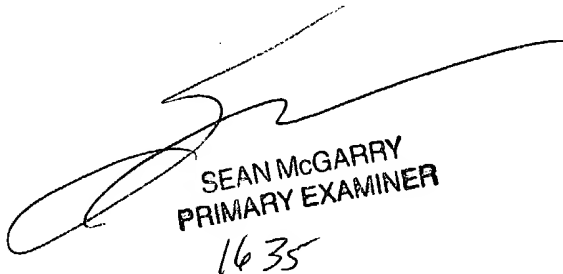
the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SRM



SEAN McGARRY  
PRIMARY EXAMINER  
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